

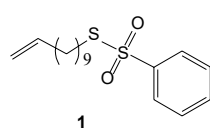
Assembling Surface Linker Chemistry with Minimization of Non-Specific Adsorption on Biosensor Materials

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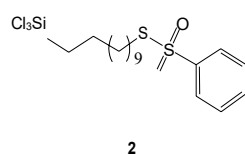
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1. Synthesis of TUBTS



S-undec-10-enyl benzenethiosulfonate 1. To a stirred solution of 11-bromo-undec-1-ene (95%, 4.6 mL, 20.1 mmol, 1.0 equiv.) in MeCN (100 mL) were added benzenethionosulfonic acid sodium salt (85%, 9.2 g, 39.9 mmol, 2.0 equiv.) at rt. After overnight refluxing, the resulting solution was submitted to a EtOAc/H₂O extraction. The combined organic phases were then dried over anhydrous Na₂SO₄, filtered and finally evaporated *in vacuo*. Purification was achieved by column chromatography (Hexanes/EtOAc gradient 100/0 to 95/5) to afford 6.15 g (93%) of a pale cloudy yellow oil (> 95% purity). An additional careful column chromatography afforded pure **1** as a pale yellow oil. **1**: ¹H NMR (300 MHz, CDCl₃) δ 7.95 (m, 2H), 7.64 (m, 1H), 7.56 (m, 2H), 5.82 (m, 1H), 5.14-4.91 (m, 2H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.04 (q, *J* = 7.0 Hz, 2H), 1.58 (qt, *J* = 7.2 Hz, 2H), 1.42-1.16 (m, 12H); ¹³C NMR (75 MHz, CDCl₃) δ 145.2, 139.4, 133.7, 129.4, 127.2, 114.4, 36.3, 34.0, 29.5, 29.4, 29.2, 29.1, 29.0, 28.8, 28.7; IR (neat) 3070 cm⁻¹, 1640 cm⁻¹, 1328 cm⁻¹, 1147 cm⁻¹; HRMS (ESI, *m/z*) calcd. for C₁₇H₂₇S₂O₂ (MH⁺) 327.1446, found 327.1447.



S-(11-trichlorosilyl-undecenyl) benzenethiosulfonate 2 (TUBTS). In a heavy-walled tube equipped with a magnetic stirring bar, **S-undec-10-enyl benzenethiosulfonate 1** (700 mg, 2.13 mmol, 1.0 equiv.) and H₂PtCl₆·6H₂O (1 mg, 0.013 mmol, 0.1 mol. %) was placed. The tube was transferred into a glove-box and HSiCl₃ (0.30 mL, 2.94 mmol, 2.1 equiv.) was added to the solution. The tube was tightly fastened and then removed from the glove-box. The resulting solution was stirred at room temperature for 43 h behind a protecting shield. Excess HSiCl₃ was then removed under high vacuum to afford **2** as a viscous orange oil (633 mg, 95%). **2**: ¹H NMR (300 MHz, CDCl₃) δ 7.93 (m, 2H), 7.63 (m, 1H), 7.55 (m, 2H), 2.99 (t, *J* = 7.3 Hz, 2H), 1.65-1.51 (m, 4H), 1.44-1.16 (m, 16H).

Citation: Sheng, J.C.-C.; De La Franier, B.; Thompson, M. Assembling Surface Linker Chemistry with Minimization of Non-Specific Adsorption on Biosensor Materials. *Materials* **2021**, *14*, 472. <https://doi.org/10.3390/ma14020472>

Received: 17 December 2020

Accepted: 13 January 2021

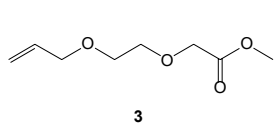
Published: 19 January 2021

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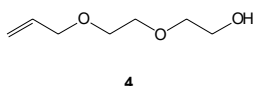


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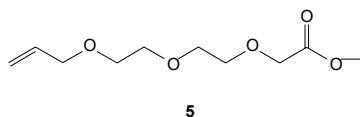
2. Synthesis of OEG-TUBTS



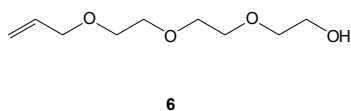
(2-allyloxy-ethoxy)-acetic acid methyl ester 3. To a stirred solution of 2-allyloxy-ethanol (5.5 mL, 50.0 mmol, 1.0 equiv.) in THF (50 mL) was carefully added NaH (60%, 2.4 g, 60.0 mmol, 1.2 equiv.) in small portions at rt. The solution was then refluxed for 1 h (until H₂ release ceases). After cooling to 0°C, the resulting solution is added dropwise to a stirred solution of Methyl bromoacetate (5.7 mL, 60.0 mmol, 1.2 equiv.) in THF (50 mL). After completion (30 min at 0°C), the resulting solution was submitted to an EtOAc/H₂O extraction. The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, then filtered and evaporated *in vacuo*. Purification was achieved by column chromatography (Hexanes/EtOAc gradient 95/5 to 60/40). **3**: yellow oil (6.66 g, 70%); ¹H NMR (400 MHz, CDCl₃) δ 5.96–5.85 (m, 1H), 5.31–5.24 (m, 1H), 5.20–5.15 (m, 1H), 4.17 (s, 2H), 4.04–4.01 (m, 2H), 3.75 (s, 3H), 3.75–3.72 (m, 2H), 3.65–3.62 (m, 2H); ¹³C NMR (100MHz, CDCl₃) δ 171.1, 134.8, 117.3, 72.4, 71.2, 69.7, 68.9, 51.9; IR (neat) 1755 cm^{−1}; HRMS (ESI, *m/z*) calcd. For C₈H₁₅O₄ (MH⁺) 175.0964, found 175.0960.



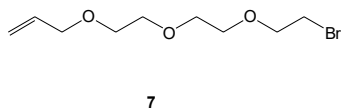
2-(2-allyloxy-ethoxy)-ethanol 4. To a stirred solution of ester **3** (9.77 g, 55.1 mmol, 1.0 equiv.) in THF (100 mL) was carefully added one portion of LAH (1.10 g, 27.5 mmol, 0.5 equiv.) at 0°C. After 30 min, another portion of LAH was carefully added and then the reaction was stirred for an extra 30 min. The reaction was then carefully quenched with a dropwise addition of a Na₂SO₄ saturated aqueous solution. White aluminum salts were then filtered off over a short plug of Celite (EtOAc washings) and the resulting filtrate was finally evaporated *in vacuo*. Purification was achieved by distillation under reduced pressure using a Kugelrohr distillation apparatus to afford **4** as a colourless oil (7.99 g, 99%). Spectroscopic data was consistent with those reported in the literature:⁸¹ ¹H NMR (400 MHz, CDCl₃) δ 5.92 (ddt, *J* = 17.3, 10.4, 5.6 Hz, 1H), 5.29 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.20 (dq, *J* = 10.4, 1.6 Hz, 1H), 4.04 (dt, *J* = 5.6, 1.6 Hz, 2H), 3.76–3.73 (m, 2H), 3.71–3.68 (m, 2H), 3.64–3.60 (m, 4H), 2.36 (brs, 1H).

**(2-(2-allyloxy-ethoxy)-ethoxy)-acetic acid methyl ester 5.**

To a stirred solution of alcohol **4** (4.86 g, 33.2 mmol, 1.0 equiv.) in THF (35 mL) was carefully added NaH (60%, 1.60 g, 40.0 mmol, 1.2 equiv.) in small portions at rt. The solution was then refluxed for 1 h (until H₂ release ceases). After cooling to 0°C, the resulting solution is added dropwise to a stirred solution of Methyl bromoacetate (5.7 mL, 60.0 mmol, 1.2 equiv.) in THF (35 mL). After completion (30 min at 0°C), the resulting solution was submitted to an EtOAc/H₂O extraction. The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, and then filtered and evaporated *in vacuo*. Purification was achieved by distillation under high vacuum. **5**: colourless oil (5.49 g, 75%); bp = 130–140 0°C (0.09 Torr); ¹H NMR (300 MHz, CDCl₃) δ 5.98–5.84 (m, 1H), 5.32–5.24 (m, 1H), 5.22–5.14 (m, 1H), 4.17 (s, 2H), 4.02 (m, 2H), 3.75 (s, 3H), 3.75–3.58 (m, 8H); ¹³C NMR (75 MHz, CDCl₃) δ 171.0, 134.8, 117.1, 72.3, 71.0, 70.8, 70.7, 69.5, 68.7, 51.8; IR (neat) 1754 cm^{−1}; HRMS (ESI, *m/z*) calcd. for C₁₀H₁₉O₅ (MH⁺) 219.1236, found 219.1227.

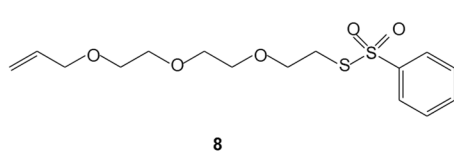
**2-(2-(2-allyloxy-ethoxy)-ethoxy)-ethanol 6.**

To a stirred solution of ester **5** (4.60 g, 21.1 mmol, 1.0 equiv.) in THF (60 mL) was carefully added one portion of LAH (0.50 g, 12.5 mmol, 0.5 equiv.) at 0°C. After 30 min, another portion of LAH was carefully added. The reaction was then stirred for an extra 30 min. The reaction was carefully quenched with a dropwise addition of a Na₂SO₄ saturated aqueous solution. White aluminum salts were then filtered off over a short plug of Celite (EtOAc washings) and the resulting filtrate was finally evaporated *in vacuo* to afford pure **6** (no purification required) as a pale yellow oil (3.89 g, 97%). Spectroscopic data were consistent with those reported in the literature:⁸¹ ¹H NMR (300 MHz, CDCl₃) δ 5.93 (ddt, *J* = 17.2, 10.3, 5.7 Hz, 1H), 5.28 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.19 (dq, *J* = 10.3, 1.5 Hz, 1H), 4.04 (dt, *J* = 5.7, 1.5 Hz, 2H), 3.78–3.58 (m, 12H), 2.51 (brs, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 134.8, 117.3, 72.7, 72.4, 70.8, 70.7, 70.5, 69.5, 61.8.

**3-(2-(2-(2-bromo-ethoxy)-ethoxy)-ethoxy)-prop-1-ene 7.**

To a stirred solution of alcohol **6** (3.83 g, 20.1 mmol, 1.0 equiv.) and pyridine (0.16 mL, 2.00 mmol, 0.1 equiv.) in Et₂O (20 mL) was added dropwise phosphorus tribromide (0.74 mL, 7.60

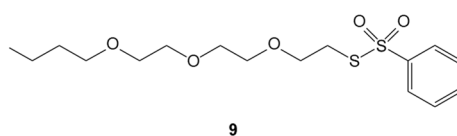
mmol, 0.36 equiv.) at 0°C. After 30 min at 0°C, the reaction was allowed to warm to room temperature. As the reaction was apparently not complete after 12h of stirring, pyridine (1.60 mL, 20.0 mmol, 1.0 equiv.) and sodium bromide (4.14 g, 40.2 mmol, 2.0 equiv.) were added successively. After 12h of reflux, the resulting solution was submitted to an EtOAc/NH₄Cl saturated aqueous solution extraction. The combined organic phases were then dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo*. Purification was achieved by column chromatography (Hexanes/EtOAc gradient 95/5 to 60/40). **7**: yellow oil (0.90 g, 18%); ¹H NMR (300 MHz, CDCl₃) δ 5.93 (ddt, *J* = 17.3, 10.5, 5.7 Hz, 1H), 5.28 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.19 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.03 (dt, *J* = 5.7, 1.5 Hz, 2H), 3.82 (t, *J* = 6.3 Hz, 2H), 3.71–3.65 (m, 6H), 3.64–3.59 (m, 2H), 3.48 (t, *J* = 6.3 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 134.9, 117.4, 72.5, 71.4, 70.9, 70.8, 70.7, 69.6, 30.5.



S-(2-(2-(2-allyloxy-ethoxy)-ethoxy)-ethyl) benzenethiosulfonate 8. To a stirred solution of bromide **7** (0.90 g, 3.6 mmol, 1.0 equiv.) in MeCN (18 mL) was added

benzenethiosulfonic acid sodium salt (85%, 1.64 g, 7.1 mmol, 2.0 equiv.) at rt. After overnight refluxing, the resulting solution was submitted to an EtOAc/brine extraction. The combined organic phases were then dried over anhydrous Na₂SO₄, filtered and finally evaporated *in vacuo*. Purification was achieved by column chromatography (Hexanes/EtOAc gradient 95/5 to 30/70) to afford 1.04 g (84%) of a pale yellow oil (> 95% purity). An additional careful column chromatography afforded pure **8** as a pale yellow oil. **8**: ¹H NMR (300 MHz, CDCl₃) δ 7.95 (m, 2H), 7.65 (m, 1H), 7.56 (m, 2H), 5.91 (m, 1H), 5.32–5.14 (m, 2H), 4.01 (m, 2H), 3.72 (m, 10H), 3.20 (t, *J* = 6.3 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 145.0, 134.9, 133.9, 129.5, 127.2, 117.3, 72.4, 70.8, 70.7, 70.6, 69.6, 69.2, 35.9; IR (neat) 3068, 1647, 1324, 1142 cm⁻¹; HRMS (ESI, *m/z*) calcd. for C₁₅H₂₃S₂O₅ (MH⁺) 347.0971, found 347.0981.

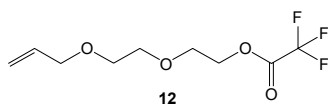
Cl₃Si



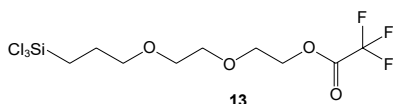
S-(2-(2-(2-(3-trichlorosilyl-propyloxy)-ethoxy)-ethoxy)-ethyl) benzenethiosulfonate 9 (OEG-TUBTS). In a heavy-walled tube

equipped with a magnetic stirring bar, benzene-thiosulfonate **8** (347 mg, 1.00 mmol, 1.0 equiv.) and H₂PtCl₆·6H₂O (1 mg, 0.002 mmol, 0.5 mol. %) were placed. The tube was transferred into a glove-box and HSiCl₃ (0.30 mL, 2.94 mmol, 3.0 equiv.) was added to the solution. The tube was tightly fastened and then removed from the glove-box. The resulting solution was stirred at room temperature for 21 h behind a protecting shield. HSiCl₃ excess was then removed under high vacuum to afford **9** as a viscous yellow- orange cloudy oil (444 mg, 92%). **9**: ¹H NMR (300 MHz, CDCl₃) δ 7.94 (m, 1H), 7.62 (m, 1H), 7.56 (m, 1H), 7.46 (m, 1H), 7.32 (m, 1H), 3.85–3.52 (m, 16H), 3.20 (t, *J* = 6.2 Hz, 1H), 2.80 (t, *J* = 6.2 Hz, 1H).

3. Synthesis of 10-OEG-TFA



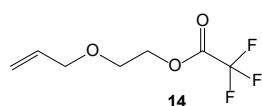
Trifluoroacetic acid 2-(2-allyloxy-ethoxy)-ethyl ester 12. To a stirred solution of alcohol **4** (2.92 mL, 20.0 mmol, 1.0 equiv.), triethylamine (5.6 mL, 40.0 mmol, 2.0 equiv.) and 4-DMAP (0.25 g, 2.0 mmol, 0.1 equiv.) in CH₂Cl₂ (40 mL) was added dropwise trifluoroacetic anhydride (3.37 mL, 24.0 mmol, 1.2 equiv.) at 0°C. The solution was then allowed to warm to room temperature and then stirred overnight. The resulting solution was submitted to a CH₂Cl₂/saturated NH₄Cl aqueous solution extraction. The combined organic phases were dried over anhydrous Na₂SO₄, filtered then evaporated *in vacuo*. Purification was achieved by distillation under reduced pressure. **12**: colourless oil (3.61 g, 70%); bp = 100–110°C (water tap vacuum); ¹H NMR (400 MHz, CDCl₃) δ 5.91 (ddt, *J* = 17.2, 11.6, 5.6 Hz, 1H), 5.27 (dq, *J* = 17.2 Hz, 1H), 5.18 (dq, *J* = 11.6, 1H), 4.50 (t, *J* = 4.8 Hz, 2H), 4.02 (dt, *J* = 5.6 Hz, 2H), 3.80 (t, *J* = 4.8 Hz, 2H), 3.64 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 157.8 (q, *J* = 42.4 Hz), 134.2, 117.7, 114.8 (q, *J* = 283.9 Hz) 72.2, 71.0, 68.7, 67.8 66.2.



Trifluoroacetic acid 2-(2-(3-trichlorosilyl)propoxy)-ethoxy)-ethyl ester 15 (10-OEG-TFA). In a heavy-walled tube equipped with a

magnetic stirring bar, OEG-diluent precursor **12** (0.50 g, 1.9 mmol, 1.0 equiv.) and H₂PtCl₆·6H₂O (1 mg, 0.002 mmol, 0.1 mol. %) were placed. The tube was transferred into a glove-box and HSiCl₃ (0.39 mL, 3.8 mmol, 2.0 equiv.) was added to the solution. The tube was tightly fastened then removed from the glove-box. The resulting solution was stirred at room temperature for 20 h behind a protecting shield. HSiCl₃ excess was then removed under high vacuum to afford **13** as an orange-brown oil (0.67 g, 90%). **13**: ¹H NMR (400 MHz, CDCl₃) δ 4.50 (m, 2H), 3.79 (m, 2H), 3.65 (m, 4H), 3.51 (m, 2H), 1.85 (m, 2H), 1.47 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 157.6 (q, *J* = 42.4 Hz), 114.2 (q, *J* = 284.0 Hz), 71.8, 70.6, 70.2, 68.1, 66.5, 22.2, 20.8.

4. Synthesis of 7-OEG-TFA



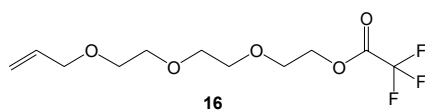
Trifluoroacetic acid 2-allyloxy-ethyl ester 10. To a stirred solution of 2-allyloxy-ethanol (4.36 mL, 40.0 mmol, 1.0 equiv.), triethylamine (11.2 mL, 80.0 mmol, 2.0 equiv.) and 4-

DMAP (0.49 g, 4.0 mmol, 0.1 equiv.) in CH₂Cl₂ (80 mL) was added dropwise trifluoroacetic anhydride (6.74 mL, 48.0 mmol, 1.2 equiv.) at 0°C. The solution was then allowed to warm to room temperature then stirred overnight. The resulting solution was submitted to a CH₂Cl₂/saturated NH₄Cl aqueous solution extraction. The combined organic phases were dried over anhydrous Na₂SO₄, filtered then evaporated *in vacuo*. Purification was achieved by distillation under reduced pressure. **10**: colourless oil (5.76 g, 72%); bp = 72–74°C (water tap vacuum); ¹H NMR (400 MHz, CDCl₃) δ 5.88 (m, 1H), 5.29 (brd, *J* = 17.2 Hz, 1H), 5.20 (m, 1H), 4.50 (t, *J* = 4.8 Hz, 2H), 4.03 (m, 2H), 3.73 (t, *J* = 4.8 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 157.7 (q, *J* = 4.1 Hz), 134.2, 117.8, 114.7 (q, *J* = 283.9 Hz), 72.4, 67.2, 67.0.

15. Trifluoroacetic acid 2-(3-trichlorosilyl-propyloxy)- ethyl ester (7-OEG-TFA).

In a heavy-walled tube equipped with a magnetic stirring bar, OEG-diluent precursor **10** (3.97 g, 20.0 mmol, 1.0 equiv.) and $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$ (104 mg, 0.20 mmol, 1.0 mol. %) were placed. The tube was transferred into a glove-box and HSiCl_3 (4.10 mL, 40.2 mmol, 2.0 equiv.) was added to the solution. The tube was tightly fastened then removed from the glove-box. The resulting solution was stirred at room temperature for 20 h behind a protecting shield. Purification was achieved by Kugelrohr distillation under high vacuum. **11**: colourless oil (5.46 g, 82%); bp = 115–120 °C (0.09 Torr); ^1H NMR (400 MHz, CDCl_3) δ 4.50 (m, 2H), 3.73 (m, 2H), 3.54 (t, J = 6.2 Hz, 2H), 1.85 (m, 2H), 1.48 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.7 (q, J = 42.4 Hz), 114.3 (q, J = 284.0 Hz), 71.8, 67.9, 67.0, 22.8, 21.0.

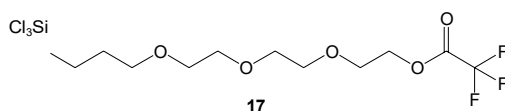
5. Synthesis of 13-OEG-TFA



Trifluoroacetic acid 2-(2-(2-allyloxy-ethoxy)-ethoxy)-ethyl ester **16.** To a stirred solution of alcohol **6** (1.92 mL, 10.0 mmol, 1.0 equiv.),

triethylamine (2.8 mL, 20.0 mmol, 2.0 equiv.) and 4-DMAP (0.13 g, 1.0 mmol, 0.1 equiv.) in CH_2Cl_2 (20 mL) was added dropwise trifluoroacetic anhydride (1.69 mL, 12.0 mmol, 1.2 equiv.) at 0°C. The solution was then allowed to warm to room temperature then stirred overnight. The resulting solution was submitted to a CH_2Cl_2 /saturated NH_4Cl aqueous solution extraction. The combined organic phases were dried over anhydrous Na_2SO_4 , filtered then evaporated *in vacuo*. Purification was achieved by distillation under high vacuum then followed by a quick column chromatography (CH_2Cl_2 /EtOAc gradient 100/0 to 95/5).

16: pale yellow oil (1.72 g, 60%); bp = 140–150°C (water tap vacuum); ^1H NMR (400 MHz, CDCl_3) δ 5.91 (J = 17.2, 10.4, 5.6 Hz, 1H), 5.27 (dq, J = 17.2, 1.6 Hz, 1H), 5.17 (dq, J = 10.4, 1.6 Hz, 1H), 4.49 (t, J = 4.8 Hz, 2H), 4.02 (dt, J = 5.6 Hz, 2H), 3.79 (t, J = 4.8 Hz, 2H), 3.69–3.58 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.8 (q, J = 42.4 Hz), 134.3, 117.5, 114.8 (q, J = 283.8 Hz), 72.2, 70.8, 70.7, 70.6, 69.4, 68.2, 67.0.



Trifluoroacetic acid 2-(2-(2-(3-trichlorosilyl-propyloxy)-ethoxy)-ethoxy)-ethyl ester **17 (13-OEG-TFA).**

In a heavy-walled tube equipped with a magnetic stirring bar, OEG-diluent precursor **16** (0.50 g, 1.7 mmol, 1.0 equiv.) and $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$ (1 mg, 0.002 mmol, 0.1 mol. %) were placed. The tube was transferred into a glove-box and HSiCl_3 (0.35 mL, 3.4 mmol, 2.0 equiv.) was added to the solution. The tube was tightly fastened then removed from the glove-box. The resulting solution was stirred at room temperature for 20 h behind a protecting shield. HSiCl_3 excess was then removed under high vacuum to afford **17** as an orange-brown oil (0.64 g, 90%). **17**: ^1H NMR (400 MHz, CDCl_3) δ 4.47 (m, 2H), 3.77 (m, 2H), 3.70–3.47 (m, 10H), 1.85 (m, 2H), 1.47 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.8 (q, J = 42.6 Hz), 114.4 (q, J = 283.7 Hz), 71.9, 70.8, 70.7, 70.6, 68.2, 67.0, 65.9, 22.4, 21.0.